REMARKS

The issues outstanding in the Office Action of May 21, 2009, are the objections to the claims, and the rejections under 35 U.S.C. 112. Reconsideration of these issues, in view of the following discussion, is respectfully requested. The Examiner is thanked for indicating that claim 3 is allowable. In view of the following discussion, it is submitted that all claims are in condition for allowance.

Claim Objections

Claims 1, 2, 4, 6-9, 12 and 14-15 have been objected to, as a result of the dashed line. Inasmuch as CH is no longer present in the definition of Q, the dashed line (which originally represented a single or double bond) has now been modified to represent the single bond. Withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. 112

Claims 8 and 14 have been rejected under 35 U.S.C. 112, first paragraph as lacking written description. It is argued, at page 2 of the Office Action, that there is no guidance for an additional "medicament active ingredient." In fact, one of ordinary skill in the art clearly knows that combination medications, with two active ingredients, can be routinely formulated, and would have no problem interpreting the claim, and determining the appropriate additional active ingredients. However, in order to expedite prosecution, these claims have been cancelled. It is noted that the pharmaceutical composition claims herein, using the open-ended term "comprising", do not exclude any additional active ingredients. Withdrawal of this rejection is accordingly respectfully requested.

Claims 8, 9, 14 and 15 have been rejected under 35 U.S.C. 112, first paragraph. It is argued that there is no enablement for solvates of compounds of formula I. Applicants respectfully disagree with this analysis. Solvates are well-known in the art, and are conventionally produced. For example, Vippagunta, the article cited by the Office Action at page 4 to support the contention that solvate formation is "unpredictable," in fact provides a vast array

of solvates which are easily formed. It is moreover noted that absolute predictability is not required. However, again in order to expedite prosecution, the term "solvates" has been cancelled from the relevant claims. Withdrawal of this rejection is accordingly respectfully requested. It is noted that claim 15, subjected to this rejection, does not, in fact, recite solvates.

Claims 12 and 15 have been rejected under 35 U.S.C. 112, first paragraph. It is admitted, at page 5 of the Office Action, that the specification is enabling for the in-vitro binding of various receptors, but argued that this disclosure does not provide enablement for treatment of migraine headaches, cerebral infarctions or obsessive-compulsive disorder. (It is noted that prevention of these disorders is no longer claimed.) Applicants respectfully submit that the specification is clearly enabling for these utilities. First, at page 2, lines 4 - 11, it is taught that the compounds of formula I act as selective serotonin reuptake inhibitors, exhibit serotonin–agonistic and antagonistic properties and thus influence serotoninergic transmission. It is further stated that the compounds exhibit 5-HT agonistic action, and this statement is supported at page 11, line 18 – page 12, line 30 with a discussion of the methods used to determine these activities in the subject compounds. At this portion of the specification, it is further taught that, based on these properties, the compounds thus are useful to treat cerebral infarctions, strokes and cerebral ischaemia. Clearly, this discussion, *without more* is sufficient to establish utility of the application for purposes of §112 of the statute, as it constitutes a scientifically supportable statement of utility which would be plausible to one of ordinary skill in the art.

It is well established that an unsupported suggestion that reactants within a class defined by claims in a typical method of use application would not work, or that such claims embrace inoperative members, is insufficient basis alone for rejecting the claims. See *Ex parte Janin*, 209 U.S.P.Q. 761 (POBA 1979). In fact, it is clear that recitations in an Applicants' specification *must* be taken by the PTO as an assertion that all compounds encompassed in the claims are operative in the invention, in the absence of reasons or evidence to the contrary. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971).

The first paragraph of 35 U.S.C §112 requires only *objective* enablement. Where a specification teaches the manner and process of making and using the invention, the specification *must* be taken as sufficient under §112, unless there is reason to doubt the truth of these

statements. See *Marzocchi, supra*. Applicants' specification clearly enables one to make and use the disclosed compounds in the claimed methods, as evidenced from the disclosure at page 15 - 16 setting forth pharmaceutical formulations and dosages and the examples which also detail the production of a pharmaceutical formulations.

On the one hand, it is submitted that the Examiner has not provided any such reasons or evidence to doubt the assertion of utility in the specification and, thus, the further steps of the analysis as set forth in *Marzocchi* are not reached. Further, in this regard, it is important to note, as a matter of law, that it is not necessary for Applicants' *method* claims to exclude inoperative embodiments, inasmuch as the claims are interpreted in light of the level of understanding one of ordinary skill in the art and, for methods, are interpreted to be *per se* functional. See *In re Angstadt*, 190 U.S.P.Q. 214 (CCPA 1976) and *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (CCPA 1974). These cases state that, for method claims, inoperative embodiments are not encompassed therein and the only question is whether it would be undue experimentation for one of ordinary skill in the art to determine the *scope* of the claim. This issue is discussed more fully below.

Thus, the only way that the issue of "undue experimentation" come up is if the PTO were to furnish reasons or evidence why the objective enablement of the present specification fails or it is alleged it would have been undue experimentation to determine the *scope* of the present method claims. The latter allegation has not been advanced, and as for the former, the only argument against enablement given is the allegation at page 6 of the Office Action that an admittedly dissimilar drug has been placed in clinical trials. This is not seen to advance the Office Action's case, inasmuch as the drug is dissimilar, and moreover, the fact that it is in clinical trials suggests that drugs having action against the stated diseases are, in fact, extant.

Moreover, with respect to the "Wands factors" discussed at length at pages 5-7 of the Office Action, these factors do not necessitate a conclusion of non-enablement. For example, with respect to the state of the art and predictability, *absolute* predictability has never been required. With respect to the guidance given by the instant specification, is submitted that the guidance is adequate, inasmuch as pharmaceutical formulation information is given, one of ordinary skill in the art can clearly prepare the compounds for administration, dosages are given and the pharmaceutical art is well developed and administration of a compound for a given indication is quite routine. The

discussion at pages 7 and 8 of the Office Action appears to be speculation on the part of the PTO that mechanisms are not well understood, however, elucidation of a mechanism is *not* necessary, where sufficient instruction is given to administer the compounds to produce the desired effect. Thus, it is submitted that this is also a non-issue. With respect to working examples, it is well established that working examples are *not* required to provide enablement. See, for example, *In re Borkowski*, 164 U.S.P.Q. 642 (CCPA 1970). With respect to the state of the art, the noted inhibitors are well known to be implicated in signaling pathways which are instrumental in the noted diseases, as discussed in the specification. Thus, it is again not seen that this is an issue.

In conclusion, it is submitted that the *Wands* factors clearly do not result in undue experimentation in order to determine whether a given cancer and/or autoimmune disease and/or a compound is within the scope of the present claims. Thus, objective enablement is clearly present, and withdrawal of the rejection under 35 U.S.C §112 is respectfully requested.

Finally, claims 4, 8 and 14 have been rejected under 35 U.S.C. 112, second paragraph. It is argued, at page 8 of the Office Action, that steps are omitted in the claims. Claims 8 and 14 have been canceled. With respect to claim 4, the claim has been clarified as fully supported in the specification at page 7, lines 1-9, and page 8, line 17. Accordingly, withdrawal of this rejection is respectfully requested.

The claims of the application are submitted to be in condition for allowance. However, if the Examiner has an questions or comments, he is cordially invited to telephone the undersigned at the number below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Harry B. Shubin/

Harry B. Shubin, Reg. No. 32,004
Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: MERCK-3099

Date: September 21, 2009